

AMENDMENTS TO THE SPECIFICATION:

Please replace paragraphs [001] and [002] with the following revised paragraphs:

[001] The present invention is related to an apparatus and method for controlling temperature in a reaction vessel. More particularly, the invention relates to Point-of-Care [(["POC"])] ("POC") analytical devices with thermal regulation of reactants in a cartridge for body fluid diagnostics. The invention uses a localized heat source ~~capable of emitting electromagnetic radiation, such as light emitting diodes ("LED"s) and vertical cavity surface emitting lasers ("VCSEL"s), capable of generating internal heat, such as resistive, inductive and Peltier heaters, or capable of external heating.~~ The heat source may be a heat generator, such as resistive heaters (using directly or inductively generated current) or Peltier heaters, placed internal or external to the cartridge, or it may generate heat directly through absorption of electromagnetic radiation from, for example, light emitting diodes ("LEDs") or vertical cavity surface emitting lasers ("VCSELs").

[002] Conducting chemical reactions on the microscopic scale in a miniature analytical device, while being able to precisely vary reaction parameters such as concentration and temperature ~~[[have]]~~ has been made possible by trends in microfluidics and combinatorial chemistry. Such control requires thermal regulation using a localized heat source on the miniature analytical device.

Please replace paragraph [004] with the following revised paragraph:

[004] The term “localized heat source” refers to a source of heat which is proximate to the substance to be heated. Such a source can comprise [[of]] multiple point sources of heat. One particular area [[where]] in which being able to carry out chemical and biological reactions on a miniature device in the field has great importance is the area of medical diagnostics of bodily fluids such as blood.

Please replace paragraph [006] with the following revised paragraph:

[006] The home-care or self-analysis by patients [[had]] has been facilitated by miniature analytical devices, ~~which~~ that can analyze body fluids. Many POC tests are performed using capillary whole blood. Typically, a drop of blood for analysis is obtained by making a small incision in the fingertip or forearm, creating a small wound, which generates a small blood droplet on the surface of the skin. Moving tests closer to the patient’s side by using miniature analytical devices, improves both the testing process and the clinical data information management, which in turn has a dramatic impact on both patient outcomes and costs to the health care system.

Please replace paragraphs [009] and [010] with the following revised paragraphs:

[009] Thermal regulation of reactants or assay elements can be achieved through bulk heating of the cartridge using heaters such as electrical resistance heaters, Peltier heating and cooling cells, air heaters, or infrared heaters. These

bulk-heating systems are usually large, and have generous energy supplies. POC devices require smaller volumes than bench-top systems. POC device volumes range between 1×10^{-1} and 1×10^3 microliters. More specifically, a POC diagnostic ~~devices~~ device can heat volumes of 1-5 micro liters of assay elements, such as a blood sample, and/or 100-500 micro liters of assay elements, such as reagents. Restricting the volume to be heated to the temperature-controlled zones reduces the amount of heat required and facilitates localized heating.

[010] For a POC device to be truly portable, power management is a critical issue. One method of limiting power usage is to localize heating to only those zones where heating is necessary. Localized heating provides lower power consumption and more rapid attainment of a specified reaction temperature. Such a localized approach to heating has the added benefit of minimizing the cost of manufacturing the disposable cartridge for diagnostic analysis. The localized heating elements needed for the rapid transmission of heat and the regulation of temperature can be ~~localized~~ located on the POC device and the assay elements to be heated can be ~~localized~~ located on the disposable cartridge. Such efficiencies in power usage can save battery life.

Please replace paragraph [013] with the following revised paragraph:

[013] In accordance with the invention, a miniature analytical device with thermal regulation comprises ~~[[of]]~~ a localized heat source to regulate the temperature in an array of temperature-controlled zones containing reactants such

as assay elements for body fluid analysis. Thermal regulation through electromagnetic radiation can be achieved through the absorbance of irradiation by molecules of the reactants or assay elements, for example, the water molecules in the body fluid sample. Electromagnetic radiation can be emitted by LEDs, VCSELs, or microwave sources. Resistive, inductive and Peltier heaters positioned within or adjoining the reactants can generate internal heat. External heat can be generated by resistive heaters in contact with the cartridge which in turn heat the reactants.

Please replace paragraph [023] with the following revised paragraph:

[023] Similarly, each reactant can require a specified thermal regulation depending on the particular assay. The electromagnetic radiation emitter can be configured into an array of point sources of electromagnetic radiation. The miniature analytical device and the array of point sources of electromagnetic radiation allows many assays to be run simultaneously on one cartridge using a variety of reactants. In one embodiment, a variety of assays can be run using pre-packaged assay elements, such as reagents, and one recently obtained assay element, such as blood.

Please replace paragraph [025] with the following revised paragraph:

[025] VCSELs can be formed by using for example a GaInAs, GaAlInP, Fabry-Perot, or ZnSe material system to generate infrared light at wavelengths of, for

example, 980 nanometers and a beam diameter of 8-10 micrometers. The VCSELs are constructed on chips with, for example, grown diamond, AlN or plain copper substrates to control the incidental heat flux created on the miniature analytical device by generating the infrared light. VCSELs have 15-50% conversion efficiency between the power it takes to run the VCSEL to the infrared power generated. Moreover, VCSELs allow for measurement of the concentration of compounds by optical tests known in the art. The cartridge can be configured such that a transparent material bounds both sides of the temperature-controlled zone. On one side, the VCSEL emits infrared light to thermally regulate the reactants or assay elements. On the other side, the infrared light transmitted through the reactants or assay elements can be measured to determine the concentration of a material within the reactants. The term "material" refers to the product-of-interest of the reaction whose concentration is to be measured or the analyte within the assay elements of which the assay is testing concentration.

Please replace paragraphs [027] and [028] with the following revised paragraphs:

[027] In bench-top thermal regulation, assay elements such as blood have been heated to either 25°C or 37°C using infrared light energy. An added benefit of using optical energy such as infrared light consists of using optical means for measuring the temperature. Such means are well known in the art, and retain the benefit of non-contact between the miniature analytical device and the disposable cartridge. In one embodiment, the miniature analytical device can be configured with

an array of temperature monitors to correspond to the temperature-controlled zones. The term "temperature monitor" refers to a device for measuring the temperature of the reactants or assay elements in the temperature-controlled zone, or measuring the temperature of the portion of the cartridge surrounding the temperature-controlled zone or the environment. A feedback loop, comprising [[of]] providing the measured temperature to the controller, modulates the power supply to drive the infrared light source, so that the desired temperature is achieved with a smooth control curve and/or is maintained at the desired temperature.

[028] In one embodiment, the localized heat source comprises [[of]] internal heat that can be generated by resistive, inductive and Peltier heaters positioned within or adjoining the reactants. In one embodiment, these heaters can be arranged [[to]] in an array to correspond to the array of temperature-controlled zones. Resistive heaters use the effect of heating electrically resistive elements, by passing current through the elements. Inductive heaters use the effect of heating electrically conductive materials, such as metals, by inducing high frequency currents within the material. Peltier heaters use Peltier effect to generate heat by passing electric current through a bimetallic junction. In one embodiment, an array of electrical leads can be positioned to correspond to the array of heaters, such that the array of electrical leads on the miniature analytical device correspond to the heaters on the cartridge. In one embodiment, the heaters can comprise [[of]] discrete elements such as microbeads or filings, or continuous elements such as meshes, pads, or nets. These elements can be manufactured into the cartridge during the fabrication process to best position the elements in the vicinity of the temperature-controlled zones.